~~Claims~~
What is claimed is

1. Method for measuring the concentration of at least one component of a liquid biological sample before analysis of said sample by an in vitro diagnostic method, said component being apt to interfere with the measurement of a target analyte by means of said diagnostic method, said measuring method comprising

(a) measuring a first extinction spectrum $E_1(\lambda)$ of said liquid sample in a first selected wavelength range $\lambda = \lambda_{1,1}$ to $\lambda_{1,n}$, and

(b) fitting an approximated spectrum $\overline{E}_1(\lambda)$ to said first measured extinction spectrum $E_1(\lambda)$, said approximated spectrum $\overline{E}_1(\lambda)$ being a combination of

a predetermined approximation function $E_{d1}(\lambda, a_{i,s1})$ for the background extinction, with $a_{i,s1}$ being coefficients and i ranging from zero to at least one, and

a predetermined extinction spectrum $E_{s1}(C_{s1}, \lambda)$ of a first pure component of concentration C_{s1} of the components to be determined,

said fitting being performed by varying said concentration C_{s1} of said first interfering component and at least two of said coefficients $a_{i,s1}$, so that the deviation between said first measured extinction spectrum $E_1(\lambda)$ and said approximated spectrum $\overline{E}_1(\lambda)$ is minimized in order to determine the concentration of said first interfering component, and said first selected wavelength range being so selected that the concentration C_{s1} of said first interfering component can be determined unambiguously.

2. A method according to claim 1, wherein said approximated spectrum $\overline{E}_1(\lambda)$ is the sum of

said predetermined approximation function $E_{d1}(\lambda, a_{i,s1})$ for the

background extinction, and

said predetermined extinction spectrum $E_{S1}(C_{S1},\lambda)$ of said pure first component of concentration C_{S1}.

3. A method according to claim 1 or 2, characterized in that it further comprises

(a) measuring at least one further extinction spectrum $E_2(\lambda)$ of said liquid sample in at least one further selected wavelength range $\lambda = \lambda_{k,1}$ to $\lambda_{k,n}$, with $k \geq 2$, and

(b) fitting at least one further approximated spectrum $\overline{E}_2(\lambda)$ to said at least one further measured extinction spectrum $E_2(\lambda)$, said at least one further approximated spectrum $\overline{E}_2(\lambda)$ being a combination of

a predetermined approximation function $E_{dk}(\lambda,a_{i,sk})$ for the background extinction, with i ranging from zero to at least one,

previously determined extinction spectra $E_{SL}(C_{SL},\lambda)$, with L varying from L=1 to k-1, of k-1 pure components previously determined, and

a predetermined extinction spectrum $E_{Sk}(C_{Sk},\lambda)$ of a k-th pure component of concentration C_{Sk} to be determined,

said fitting being performed by varying the concentration C_{Sk} and at least two of the coefficients $a_{i,sk}$ so that the deviation between measured spectrum and approximated spectrum is minimized, in order to determine the concentration of the second component, said at least one further selected wavelength range being so selected that the concentration C_{Sk} of said k pure component can be determined unambiguously.

4. A method according to claim 3, wherein said approximated spectrum $\overline{E}_k(\lambda)$ is the sum of

said predetermined approximation function $E_{dk}(\lambda, a_{i,sk})$ for

the background extinction,
said previously determined extinction spectra $E_{SL}(C_{SL}, \lambda)$, with L varying from L=1 to k-1, of k-1 pure components previously determined, and
said predetermined extinction spectrum $E_{Sk}(C_{Sk}, \lambda)$ of said k pure component of concentration C_{Sk}.

5. A method according to claims 1 to 4, characterized in that at least one, and preferably all, of the functions $E_{dk}(\lambda, a_{i,sk})$ with $k \geq 1$, are of the form

$$f_k(\lambda, a_{i,k}) = \sum_{i=0}^{n} a_{i,k}\, \lambda^i$$

with $n \geq 1$ and preferably n=1.

6. A method according to one of claims 1 to 5, characterized in that said fitting of said approximated spectra $\overline{E}_k(\lambda)$, with $k \geq 1$, to said the measured values of extinction spectra $E(\lambda_i)$, with i=1 to N, N being the number of measured values, is done by a least squares fitting method.

7. A method according to one of claims 1 to 6, characterized in that the sample is marked at least anomalous if the determined concentrations C_{Sk} with $k \geq 1$ are outside a predetermined range.

8. A method according to one of claims 1 to 7, characterized in that a differential spectrum

$$E_{diff}(\lambda) = E(\lambda) - \sum_{j=1}^{J} \overline{E}_j(C_j, \lambda) ,$$

with J being the number of components, and
λ being in a range covering at least 30 %, preferably at least 50 %, and most preferably about 100 % or more of the whole wavelength range defined by the broadest combination

of $\lambda_{1,1}$ and $\lambda_{1,n}$, $\lambda_{2,1}$ and $\lambda_{2,n}$,..., $\lambda_{J,1}$ and $\lambda_{J,n}$ is computed, and the differential spectrum is subjected to an analysis in view of anomalies.

9. A method according to claim 8, characterized in that the curvature and/or the slope of the differential spectrum in at least one predetermined wavelength range is/are determined, the result compared with the expected values, and in that the differential spectrum is estimated to be normal if the values compared have identical sign, optionally with the magnitude resting in a predetermined range given by an upper and a lower limiting curve.

10. A method according to one of claims 1 to 9, characterized in that
the sample is blood, preferably human blood, or a fluid derived therefrom,
the first wavelength range is chosen in the range of 500 to 600 nanometer, preferably from 545 to 575 nanometer, even more preferably being essentially identical with one of these ranges, the first reference spectrum $E_1(\lambda)$ being that of hemoglobin, so that the concentration C_H of hemoglobin is determinable, and
the second wavelength range is chosen in the range of 400 to 600 nanometer, preferably from 480 to 545 nanometer, even more preferably being essentially identical with these ranges, the second reference spectrum $E_2(\lambda)$ being that of bilirubin, so that the concentration C_B of bilirubin is determinable.

11. A method according to claim 10, characterized in that the lipid concentration and the overall constitution of the sample are estimated to be normal if the differential spectrum has a negative slope and/or a positive curvature.

12. A method according to one of claims 10 to 11, characterized in that the sample is estimated to be of critical condition if the concentration of bilirubin and/or hemoglobin exceed a predetermined value, and/or if the differential spectrum is anomalous.

13. A method according to one of claims 1 to 11, characterized in that the spectra are provided as electrical signals and furnished to an evaluation device comprising a processor which performs the method steps on the spectra under the control of a program, and that the results are stored in a storage means, preferably a storage means for digital data, and/or presented to an operator, preferably by printing, displaying and/or producing audible sounds.

14. An [installation] apparatus for implementing the method of one of claims 1 to 13 for use with an analyzer, preferably a clinical-chemical analyzer, characterized in that in the supply path of sample fluid of the analyzer, at least one photometric measurement site is provided so that extinction spectra can be taken of the fluid in the supply path.

15. A photometric probe for implementing the method of one of claims 1 to 13, characterized in that its end comprises a photometric measurement site confined by two facing walls, one of which being equipped with a light source, and the second [well] wall being equipped with a light capturing means, the measurement site, the light source and the light capturing means being so arranged that light emanating from the light source passes the measurement site and, at least to a significant part, is captured by the light capturing means.

16. A photometric probe according to claim 15, characterized in that it comprises a light guide passing the measurement

site, and that a light deviating means, preferably a prism, is arranged such that light exiting the light guide is deviated, preferably by an angle of substantially 180°, towards the light exiting side of the first wall of the measurement site.

17. An analyzer, preferably a chemical-clinical analyzer, with an [installation] apparatus for photometric measurements, characterized in that the [installation] apparatus comprises a program memory and a device for executing the program, wherein the execution of the program implements the method of one of claims 1 to 12.

Add A2

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